REMARKS

Entry of the foregoing, reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested.

The Office Action Summary correctly indicates that claims 17-45 were pending in the application. Claims 17-45 were subject to a restriction requirement. Claims 27-45 were withdrawn from consideration. Claims 17-26 were considered and rejected.

By the present amendment, claims 17-45 have been canceled without prejudice or disclaimer of the subject matter described therein. Claims 46-70 have been added.

New claims 46-56 are directed to the subject matter of elected Group I that previously comprised claims 17-26. Claims 46-56 have been rewritten to better describe the claimed invention and to address issues raised in the Office Action as further discussed below.

New claims 57-70 are directed to subject matter previously classified in non-elected Group II. It is understood that claims 57-70 will be withdrawn from consideration under the previously stated restriction requirement. However, each of claims 57-70 depend from and necessarily incorporate all the elements of claim 46, as former claims 27-40 of Group II depended from claim 17. Therefore, since Applicants believe that claim 46 is allowable, claims 57-70 are also believed to be free of the prior art and no further search will be required to examine claims 57-70. Applicants respectfully request that, upon a finding that claim 46 is allowable, claims 57-70 be rejoined with the elected group and examined.

New claims 46-70 are supported by the specification and original claims, at least as previously described for claims 17-45, and with further reference to page 8, lines 1-10, page 22, lines 3-8, and page 27, lines 5-7.

By the present amendment, the abstract is amended to eliminate legal phraseology and to include a phrase that refers generally to the subject matter of the elected invention.

Also, by the present amendment, the specification is replaced by a substitute specification. In the substitute specification, the abbreviation GABA is spelled in capital letters and some numerals in chemical formulae are corrected to appear as subscripts. Furthermore, an obvious error that appeared on page 8 of the English version of the application as originally filed has been corrected. In the original, a range of diameters was given as 0.1 to 2 mm^2. One skilled in the art would immediately appreciate that the superscript in "mm^2" is erroneous, because diameter is a linear parameter. Elsewhere throughout the specification, particular diameters are properly measured in mm units, for example page 22, lines 3-8, and page 27, lines 5-7. In the substitute specification, this range is properly given as 0.1 to 2 mm. A marked-up version of the specification, indicating the changes from the original English language version of the specification is also submitted.

No prohibited new matter has been introduced by way of the above amendments. Applicants reserve the right to file a continuation or divisional application on any subject matter canceled by way of this Amendment.

Objections to the Disclosure

The abstract has been objected to as containing legal phraseology. The Abstract has been amended as described above. Withdrawal of the objection is respectfully requested.

The specification has been objected to for containing instances of the abbreviation GABA in lower case. The specification has been amended to spell GABA in uppercase and to correct obvious errors. Withdrawal of the objection is respectfully requested.

Claim Objections

Claim 20 has been objected to for using the non-standard transitional phrase "consisting in." Claim 20 has been canceled, thus the objection is moot. In new claims 46-70, this and other like phrases have been rewritten to better conform to conventional usage under U.S. patent practice.

Rejections under 35 U.S.C. § 112, second paragraph

Claim 17 has been rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for recitation of "Krebs mammal solution." Claim 17 has been canceled, thus the rejection is moot. However, the term "Krebs mammal solution" is also used in the currently presented claims. Applicants respectfully direct the Examiner's attention to page 21 of the specification under the heading "Solutions and Buffers" where the composition of mammal Krebs medium is defined as used in the specification. It is respectfully submitted that one skilled in the art would understand the meaning of the term "mammal Krebs solution" as used in the claims from reading the specification.

Claims 17 and 26 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for recitation of the adjective "appropriate." Claims 17 and 26 have been canceled, thus the rejection is moot. In new claims 46-70, the claimed invention is described without reciting the adjective "appropriate."

Withdrawal of the rejections is respectfully requested.

Rejections under 35 U.S.C. § 102

Regarding Reddy and Sastry (Brain Research, 168:287-98, 1979)

Claims 17-26 were rejected under 35 U.S.C. § 102 as allegedly anticipated by Reddy and Sastry (Brain Research, 168:287-98, 1979). Claims 17-26 have been canceled. Therefore, the rejection is moot.

The rejection cannot be applied to new claims 46-70 because Reddy and Sastry fail to disclose every element of the presently claimed invention. For example, Reddy and Sastry do not teach or suggest a process of making a preparation of calibrated pieces of mammalian cerebral tissue as recited in claim 46. Reddy and Sastry describe passing minced brain tissue in Krebs-Ringer bicarbonate solution ten times through nylon bolting cloth having mesh sizes of 433 μm, 264 μm, 130 μm, and 44 μm. The resulting suspension would contain pieces of tissue with dimensions no larger than the mesh size.

The volume of a geometric cube having as its dimension 433 μm on a side(the largest mesh size used by Reddy and Sastry) is $(0.433\ mm)^3 = 0.081\ mm^3$. This is substantially smaller than the pieces of mammalian cerebral tissue prepared according to the method of claim 46 and its dependant claims. Moreover, because brain tissue is soft, it would be understood that the pieces would not actually be geometric cubes. The pieces of soft tissue would necessarily have rounded edges and corners so that the maximum average volume of the resulting pieces may be better estimated by modeling the pieces as spheres than as cubes. The volume of a sphere having a diameter as large as Reddy and Sastry's largest pore size of 0.433 mm is given by the formula $4/3\ \pi\ r^3 = 0.042\ mm^3$, which is less than 1/2 the smallest size of the calibrated pieces of mammalian cerebral tissue produced according to the method of claim 46.

Reddy and Sastry teach using cloth having smaller pore sizes than 433 μm, but do not teach or suggest larger pore sizes. Thus, Reddy and Sastry do not teach or suggest any method that would produce the calibrated pieces of mammalian cerebral material produced by the present method.

Reddy and Sastry fail to anticipate the present invention as recited in claim 46 and its dependent claim, because among other things, Reddy and Sastry fail to teach or even suggest passing pieces of tissue through at least one grid having a mesh size to produce calibrated pieces of mammalian cerebral material having a mean size between about 0.1 mm^3 and about 5 mm^3.

Furthermore, claims which depend from claim 46 recite additional distinguishing features. For example, claim 53 recites the method of claim 46, wherein cutting the one or more samples into pieces comprises cutting the one or more samples into pieces of about 1 to 2 mm^3. The Office has asserted that by teaching cutting pieces of brain in solution at about 1 ml/g that this element is met. However, this teaching by Reddy and Sastry refers only to the relative amounts of tissue and solution and not to the volume (i.e. size) of the cut pieces. Reddy and Sastry do not teach or suggest any size of the cut pieces. Rather Reddy and Sastry only teach mincing, which does not suggest a calibrated cutting or even any deliberate attempt to produce pieces of tissue of a given size.

New claim 51 recites the method of claim 46 where the mesh size is between 0.5 mm and 2 mm. New claim 52 recites the method of claim 46 where the mesh size is between about 1 mm and 2 mm. The largest pore size taught by Reddy and Sastry is 0.433 mm. Reddy and Sastry teach passing a tissue suspension through finer cloth, but do not even suggest using cloth having pore sizes as recited in the present claims.

From the foregoing, it is clear that no rejection over Reddy and Sastry can be applied to the claims as currently presented.

Regarding Helme-Guizon et al. (Eur. J. Neuroscience, 10:2231-7, 1998)

Claims 17, 18, 20, 21 and 24 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Helme-Guizon et al. (European Journal of Neuroscience, 10:2231-7, 1998). Claims 17, 18, 20, 21 and 24 have been canceled. Therefore the rejection is moot.

The rejection can not be applied to the present claims. The Office asserts that Helme-Guizon et al. teach a method of isolating the CA region of rat hippocampus and passing the cells through nylon gauze. However, the method described by Helme-Guizon et al. is a very different method directed to preparing "mossy fiber synaptosomes," which are saclike structures formed by nerve endings that remain intact after tissue homogenization. Helme-Guizon prepare a homogenate from which the synaptosomes are obtained, not calibrated pieces of tissue. Further, Helme-Guizon et al. teach using nylon gauze as a filter for the homogenate, not to produce pieces of tissue having a calibrated volume.

Further, the different methods produce qualitatively different preparations. The synaptosomes of Helme-Guizon et al. are rich only in glutamate and would not permit testing of other neurotransmitters. Mossy fiber synaptosomes are specific to hippocampus and thus the method of Helme-Guizon is not applicable to a whole-brain preparation.

More quantitatively, the Office notes that the nylon used by Helme-Guizon et al. has a mesh size of 50 μm. The Office incorrectly equates this to 0.05 mm^3. In fact, a cubic piece of tissue 50 μm on a side would have a volume of 0.05 mm * 0.05 mm * 0.05 mm = 0.000125 mm^3. Approximated as a sphere with a diameter of 0.05 mm, the tissue pieces would be about 0.000065 mm^3. This is very different from the 0.1 mm^3 and 5 mm^3 calibrated

pieces of cerebral tissue recited by claim 46. Thus, Helme-Guizon et al. do not teach or suggest a method that would produce the calibrated pieces of mammalian cerebral material produced by the present claimed methods.

Regarding Garthwaite et al. (Developmental Neuroscience, 3:90-99, 1980)

Claims 24, 25 and 26 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Garthwaite et al. (Developmental Neuroscience, 3:90-99, 1980). Claims 24, 25 and 26 have been canceled. Therefore the rejection is moot.

The rejection cannot be applied to the present claims. The Office asserts that Garthwaite et al. teach a preparation of rat cerebella in Krebs solution with the approximate dimensions of 0.4 X 0.4 mm, the slices having a third dimension of 0.38 mm. However, upon close reading of Garthwaite et al., it is apparent that these dimensions refer to separate alternative procedures. In one procedure, cerebella are chopped in two dimensions to a size 0.4 X 0.4 mm. As the cerebella were cut in only two dimensions, the third dimension would be whatever the thickness of the cerebella was at the intersection of the two cuts, which would vary. There is no suggestion that the sizes of the pieces are calibrated. In the alternative procedure, Garthwaite et al. describe slicing cerebella with a bow cutter set at 0.38 mm. This procedure would produce slices having height and width dimensions of whatever the source material had, which would vary according to the size and position of the starting material in the cutter. Again, there is no suggestion that the sizes of the pieces are calibrated.

The preparations made by the method described by Garthwaite et al. are different from the preparations made according to the methods as presently claimed, at least because Garthwaite et al. do not teach or suggest any further steps that would lead to production of calibrated pieces of mammalian of cerebral tissue as produced by the method of claim 46.

Garthwaite et al. et al do not teach or suggest a method of producing pieces of cerebral tissue of any calibrated volume. Moreover, in the first procedure described by Garthwaite et al., chopping the tissue to the dimensions would be traumatizing to the tissue so that the preparation would be very different. The second procedure described by Garthwaite et al., is a classical "slice preparation" and has very little in common with the claimed preparation.

CONCLUSION

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

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